EDs Need to Recognize and Treat Highly Infectious Pathogens

Written by Mary Beth Nierengarten

Emergency department (ED) providers need to become familiar with highly infectious pathogens that may appear in patients presenting for care and should take a good travel history that includes asking about high-risk locations and exposures as well as symptom onset and duration. In addition, physicians need to learn their institutional infection prevention and control guidelines and help, when needed, to update or revise existing guidelines.

David C. Pigott, MD, University of Alabama at Birmingham, Birmingham, Alabama, USA, spoke on ways to safely evaluate and manage patients with suspected highly infectious pathogens who present to EDs while also minimizing the safety risk to ED health care workers.

He focused on inhaled anthrax, plague, viral hemorrhagic fevers (Ebola and Marburg), and Middle East Respiratory-Syndrome (MERS) Coronavirus. These pathogens all meet criteria for being highly infectious: they have a significant potential for person-to-person transmission, may pose serious risk to people including health care workers in contact with the patient, are associated with a high morbidity and mortality despite treatment, and have no proven or effective therapies to treat them.

For the bulk of his presentation, Dr Pigott used case studies of patients with inhaled anthrax, plague, and the hemorrhagic fevers to walk participants through the clinical signs and symptoms, appropriate management, and follow-up for each. Table 1 illustrates one case study on a patient presenting with inhaled anthrax.

Dr Pigott emphasized that a first critical step in identifying a suspected highly infectious pathogen is to take a good travel history that can illuminate exposure, incubation period, and any vaccines or chemoprophylaxis.

The importance of getting a good travel history is highlighted by data demonstrating that about 4 million of an estimated 50 million (8%) people who travel from industrialized to developing countries each year seek medical care abroad or upon return home, and multiple reports of infectious diseases imported to industrialized countries [Freedman DO. Travel Epidemiology. Centers for Disease Control and Prevention. 2013].

Along with taking a good travel history, emergency physicians (EPs) also need to become familiar with the clinical presentation of these pathogens, including patterns of fever and other signs and symptoms, which can help make a differential diagnosis. Data from a large study show that most febrile patients after travel present with unspecified acute symptoms (Figure 1).

Table 1. Case Study of Patient Presenting With Inhaled Anthrax

Diagnosis	Presentation	Clinical Course	Treatment	Follow-up
Inhaled Anthrax	2 d of fever, night sweats, and rigors; rapidly deteriorates and develops respiratory failure; imaging shows bibasilar infiltrates and widened mediastinum	Blood cultures show gram-positive rods; preliminary diagnosis of *Bacillus anthracis* 2 d later; samples sent to lab that diagnoses Anthrax	Patient started on oral and intravenous antibiotics upon admission; on day 3, regimen changed to rifampin, ciprofloxacin, and clindamycin; given anthrax immunoglobulin on day 6; developed multiorgan failure requiring extensive critical care support, and died on day 12	Patient's occupation becomes key to etiology of exposure; patient made and played animal hide drums, and they tested positive for *Bacillus anthracis*

Source: Anaraki S et al. *Euro Surveill.* 2008.

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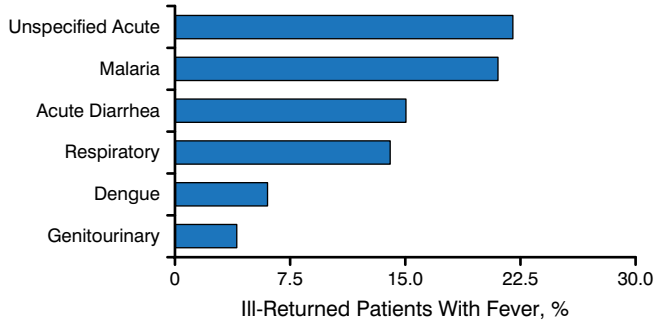
Figure 1. Many Febrile Patients Present After Travel With Unspecified Acute Symptoms (n = 6957)



Adapted from Kotylar S et al. Fever in the returning traveler. *Emerg Med Clin North Am.* 2013;31:927-944. Republished with permission of Elsevier, Inc.

To conclude, physicians should become familiar with the framework for the safe evaluation of patients with suspected highly infectious pathogens in order to effectively manage patients and at the same time minimize the risk to physicians and other health care team members.

The Challenge of Anticoagulant Reversal

Written by Toni Rizzo

Colin G. Kaide, MD, Ohio State University, Columbus, Ohio, USA, discussed the treatment of acute bleeding in patients taking old and new anticoagulants. Warfarin reversal involves 2 phases: immediate reversal and sustained reversal. Options for immediate reversal include fresh-frozen plasma (FFP), prothrombin complex concentrate (PCC), and activated PCC (aPCC) factor VIII inhibitor bypassing activity (FEIBA; Table 1).

For sustained reversal of warfarin, vitamin K must be given. Vitamin K promotes generation of the active forms of factors II, VII, IX, and X; it can be administered orally or intravenously [Ansell J et al. *Chest.* 2008].

Unfractionated heparin (UFH) can be reversed with protamine, which binds to and inactivates heparin. Protamine is administered at 1 mg/100 U UFH to a maximum dose of 50 mg. Protamine is not fully effective against low-molecular-weight heparin (LMWH). For enoxaparin reversal, protamine should be administered at 1 mg/1 mg enoxaparin if LMWH was taken within the previous 8 hours or at 0.5 mg/1 mg enoxaparin if LMWH was taken within 8 to 12 hours, up to a maximum of 50mg. Dosing should be repeated if the bleeding has not stopped and antifactor Xa levels are elevated 2 to 4 hours after the last protamine dose [Hirsh J et al. *Chest.* 2001].

One study found the anticoagulant effect of the fondaparinux was shown to be reversible in healthy volunteers with the administration of rVIIa dosed at 90 µg/kg [Bijsterveld NR et al. *Circulation.* 2002]. Another study found that rVIIa did not significantly reverse markers of anticoagulation for fondaparinux, whereas markers were likely improved with administration of PCC and completely reversed with aPCC (Feiba) [Desmurs-Clavel H et al. *Thromb Res.* 2009].

Several new oral anticoagulants (NOACs) have been developed. Among them are the direct thrombin inhibitors, dabigatran, and the direct-factor Xa inhibitors, rivaroxaban and apixaban. Reversing the action of these agents is a challenge. Hemodialysis can stop the activity of dabigatran but not of rivaroxaban and apixaban (Table 2).

Specific reversal agents for the NOACs are under development. For dabigatran, a humanized monoclonal antibody fragment is currently being investigated in several

Table 1. Options for Immediate Warfarin Reversal

Reversal Agent	Studies Regarding Agent	Dosage	Features
FFP	Holland LL et al. *Am J Clin Pathol.* 2006	10-15 mL/kg, 4 U minimum	Lowest attainable INR with FFP = 1.5
PCC	Leissinger CA et al. *Am J Hematol.* 2008	Weight-based dosing: 25-50 U/kg INR-based dosing: 2-4 = 25 U/kg; 4-6 = 35 U/kg, > 6 = 50 U/kg [Pabinger I et al. *Thromb Haemost.* 2008] Absolute dosing: INR ≤ 5 = 500 U; INR > 5 = 1000 U [Yasaka M et al. *Thromb Res.* 2005]	Mix of nonactivated clotting factors 2 types of mixes: 3-factor and 4-factor INR reversal in 15 min Corrects lab values and clinical bleeding Small risk of disease transmission Rare thromboembolic events (1.5% in 14 studies) [Leissinger CA et al. *Am J Hematol.* 2008]
aPCC (FEIBA)	Wojcik C et al. *Int J Emerg Med.* 2009	INR< 5: 500 U; INR ≥ 5: 1000 U	Contains activated factors II, VII, IX, X

aPCC, activated prothrombin concentrate; FEIBA, factor VIII inhibitor bypassing activity; FFP, fresh-frozen plasma; INR, international normalized ratio; PCC, prothrombin complex concentrate; rVIIa, activated recombinant factor VII; U, units.